THE ROLE OF DOPAMINE PATHWAY ON HUMAN SPERM: *IN VITRO* EFFECT OF DOPAMINE RECEPTOR AGONISTS AND ANTAGONISTS ON SPERM MOTILITY, KINETICS AND VIABILITY

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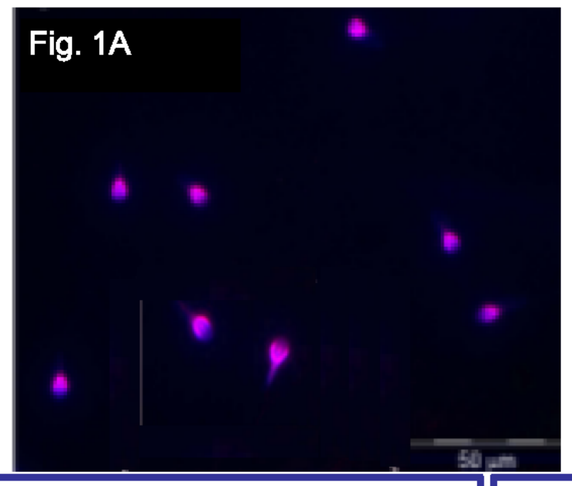
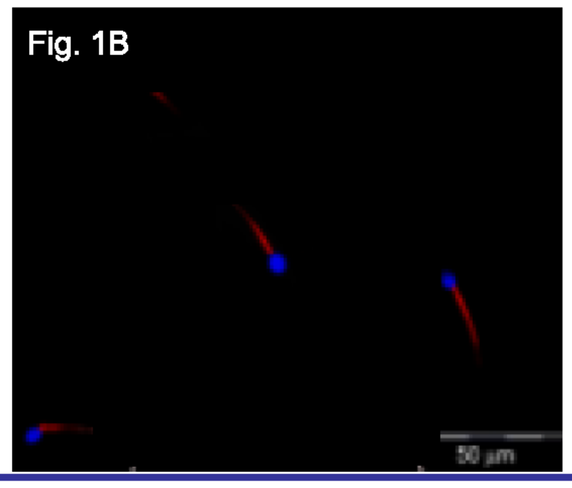
OBJECTIVES

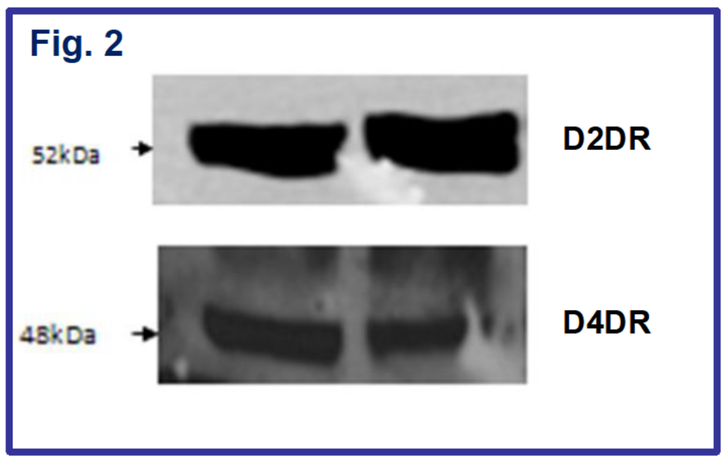
Dopamine has been found in both semen and oviductal fluid and dopamine receptors (DRs) have been detected in male genital tract and spermatozoa, suggesting that dopamine system may control important reproductive functions in humans. Dopamine improves sperm motility and viability in animal models, although the underlying molecular mechanisms have not been fully elucidated. The aims of this study were to investigate DRs expression in human spermatozoa and to evaluate the *in vitro* effects of DRs agonists and antagonists on human sperm motility, kinetics and viability.

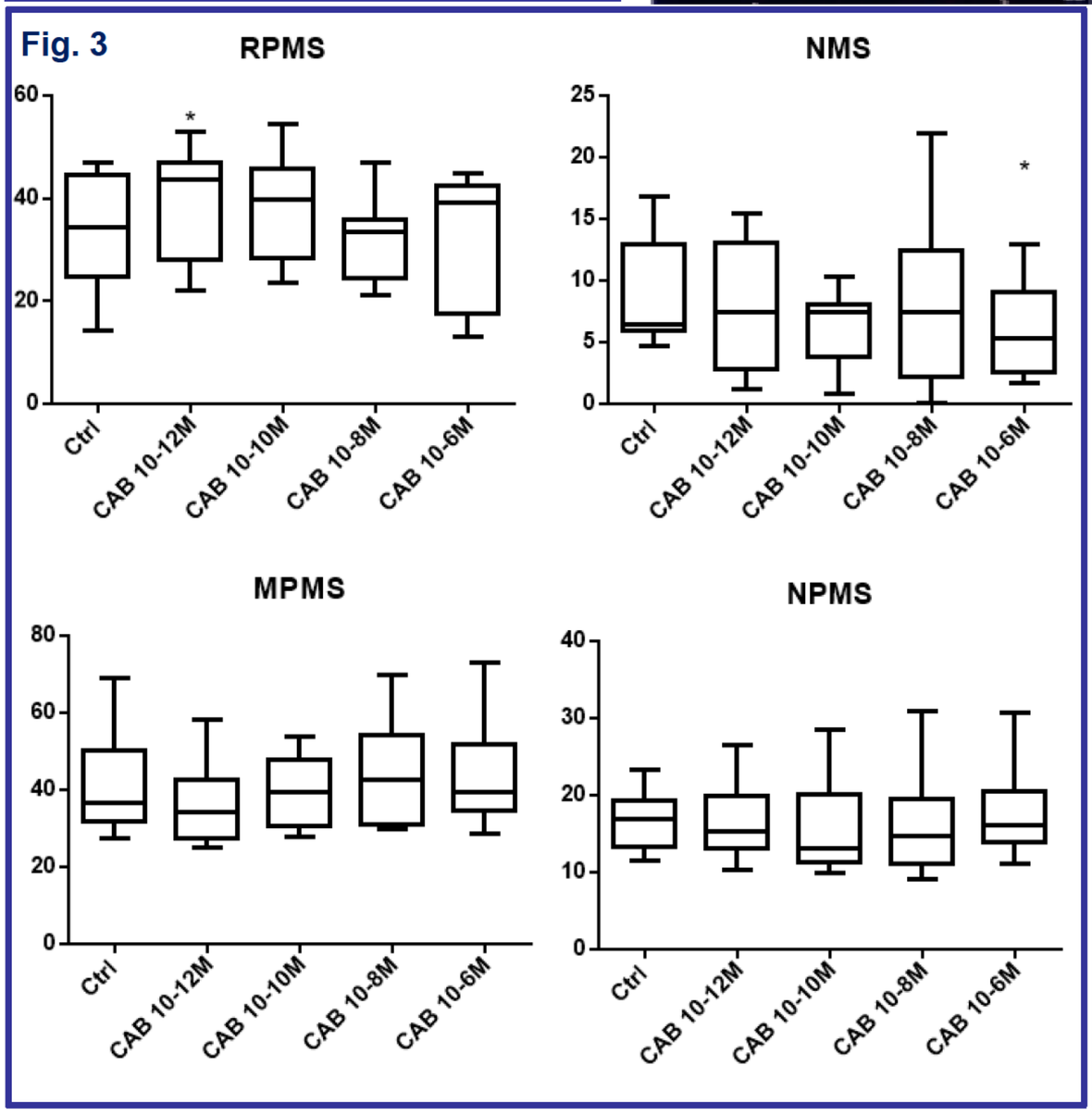
METHODS

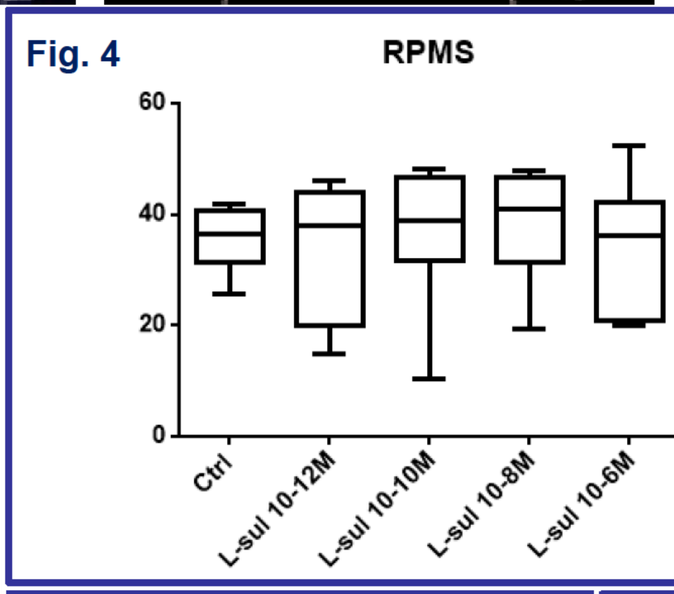
DRs expression was assessed by immunofluorescence (IF) (TRITC-conjugated antibody, nuclei counterstained in DAPI) and western blot (WB) in spermatozoa from healthy volunteers. The effects of D2DR-like agonist cabergoline (CAB), D2DR-selective antagonist L-sulpiride (L-sul), D4DR-selective agonist PD168,077 and D4DR-selective antagonist U-101958 on sperm motility, kinetics and viability were tested after 1 hour of treatment with serial doses of compounds. Sperm motility and kinetics were analyzed by Sperm Class Analyzer (SCA) 5.0, sperm viability was assessed by Vital Stain Dye. The effect of compounds on Akt activation were assessed by WB.

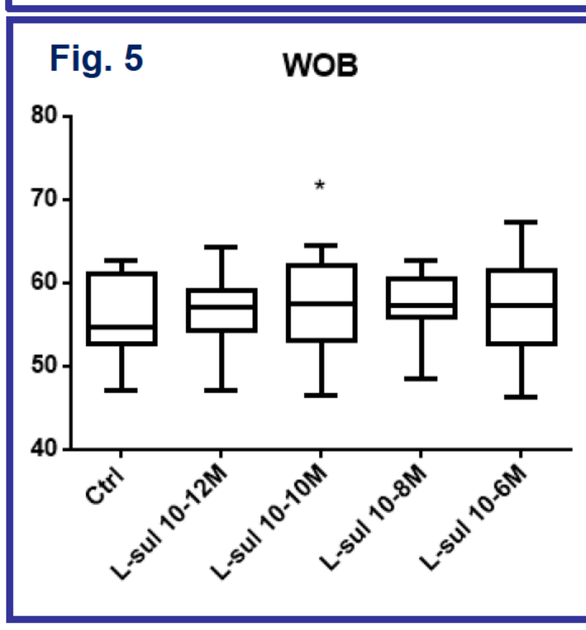


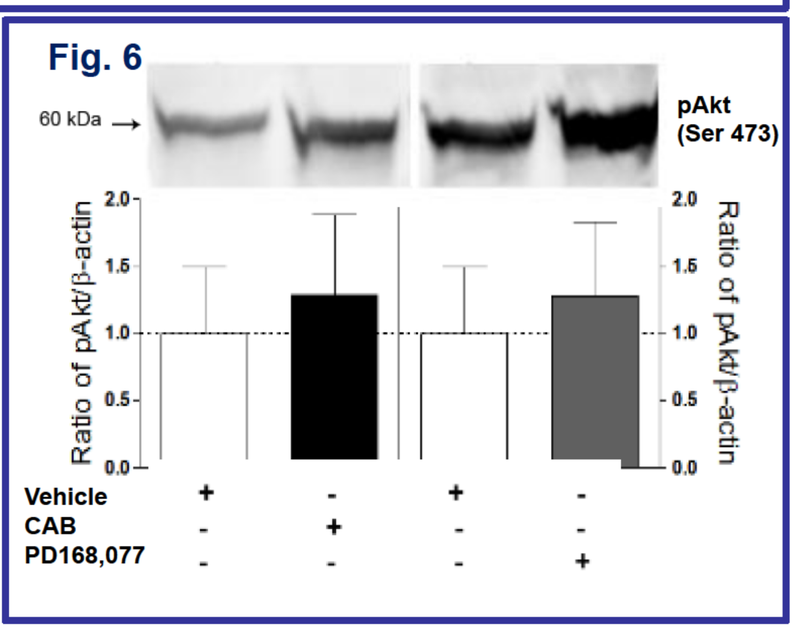












RESULTS

D2DR and D4DR are both expressed in human spermatozoa, in the post-acrosomial region (DRD2), and the middle piece and proximal tail (DRD4) (Fig. 1A and 1B, respectively), as demonstrated by IF. WB experiments confirmed the expression of both DRs in protein extracts from spermatozoa (Fig. 2 shows 2 representative samples with specific D2DR and D4DR immunoreactivity at the expected band size). After 1 hour of treatment, CAB significantly increased the percentage of rapid progressive motile spermatozoa (RPMS) and decreased the percentage of non motile spermatozoa (NMS), whereas it did not change the percentages of moderate progressive motile spermatozoa (MPMS) and non progressive motile spermatozoa (NPMS), compared to untreated samples (*$p<0.05$) (Fig. 3). L-sul showed opposite, although not significant, effects on sperm motility (Fig. 4). PD168,077 and U-101958 did not significantly change sperm motility (data not shown). Moreover, L-sul significantly increased wobble (WOB) (*$p<0.05$) (Fig5). All tested compounds did not affect sperm viability, at the time and doses tested (data not shown). Both CAB and PD168,077 induced Akt phosphorylation, compared to untreated spermatozoa (Fig. 6).

CONCLUSIONS

The results of the current study demonstrated that dopamine pathway may be involved in the modulation of human sperm motility and kinetic parameters, without affecting sperm viability, and that Akt could be regarded to as a putative mediator of such effects; however, further experiments are being performed to increase sample size and to identify the molecular mechanisms driving these effects.

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